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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,437	06/03/2005	Shoji Hara	396.45117X00	3227

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EXAMINER
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OLSON, ERIC

ART UNIT	PAPER NUMBER
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1623

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/19/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/537,437	<b>Applicant(s)</b> HARA ET AL.	
	<b>Examiner</b> Eric S. Olson	<b>Art Unit</b> 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 03 June 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-24 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>June 3, 2005</u> . | 6) <input type="checkbox"/> Other: _____  |

### **Detailed Action**

This application is a national stage application of PCT/JP03/15336, filed December 1, 2003, which claims foreign priority under 35 USC 119(a)-(d) of applications JP2002-352968, filed December 4, 2002, and JP2002-358249, filed December 10, 2002. Claims 1-24 are pending in this application and examined on the merits herein. Applicant's preliminary amendment submitted June 3, 2005 is acknowledged wherein claims 1, 3, 6, 9, 15, and 21-23 are amended and new claim 24 is introduced.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of fluorination which comprises fluorinating specific substrates identical or similar to those disclosed in examples 1-37 of the instant specification, does not reasonably provide enablement for a method of fluorination comprising fluorinating any saccharide whatsoever, or any substrate whatsoever. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: The claimed invention is a reaction method comprising fluorinating a saccharide with a fluorinating agent.

The state of the prior art: The general classes of fluorinating agents claimed in formulas I and II are known in the art as sources of nucleophilic fluorine. For example, Dmowski et al. (Reference included with PTO-892) describes the reactivity of these compounds. These compounds are shown to react with some but not all possible saccharides, or structurally similar substrates. For example, they are poor fluorinating agents against cyclohexanol, which is structurally similar to the equatorial secondary alcohols present in many saccharides. (p. 221, last paragraph) The prior art does not disclose the full range of substrates against which they are or are not effective.

The fluorinating agents included in the scope of claims 18-23 are similarly known in the art but are not characterized as to their selectivity in all possible reactions.

Microwave irradiation has been shown in the art to promote nucleophilic displacement by fluoride in fluorination reactions similar to the ones claimed, leading to

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shorter reaction times. However, the prior art does not give an reason to expect that microwaves will materially alter the scope of substrates which can be fluorinated by a particular agent, as opposed to the rate at which fluorination takes place.

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or unpredictability of the art: Many factors affect the reactivity of a particular fluorinating agent against a particular substrate, and it is not possible to predict in advance the entire scope of substrates which can serve as substrates for a particular reactant. For example, as described above, Dmowski et al. discloses that difluorobenzyl diethylamine (DBDA) is active in the fluorination of secondary acyclic alcohols such as isopropanol, but not cyclohexanol. Given the enormous diversity of chemical compounds which could theoretically be fluorinated, it is not possible to predict beforehand which ones can and cannot serve as substrates for a particular fluorinating agent. Thus the prediction of the substrate scope of a particular chemical reactant is highly unpredictable.

The Breadth of the claims: The claimed invention is extremely broad, with the term, "a substrate," encompassing any compound whatsoever to which a fluorine atom can be added by a chemical reaction. Other limitations which appear in the claims, such as "a saccharide" or "an epoxide" or "a diol" limit the claims to substrates possessing these functional groups, but still encompass a wide range of compounds and do not require that the recited functional group actually be the site of fluorination. Furthermore, the term, "saccharide" includes saccharides of any size, such as 4-, 5-, 6, and 7- carbon sugars, as well as oligo- and poly- saccharides, as well as any ring

configuration such as 5- and 6- membered rings and any arrangement of free hydroxyls, protecting groups, and further functional groups such as nuclide bases.

The amount of direction or guidance presented: Applicant's specification does not disclose a general method by which one skilled in the art could determine the entire scope of compounds capable of being fluorinated by the claimed fluorinating agent.

The presence or absence of working examples: Examples 1-37 provide a number of examples of fluorination reactions. However, the examples provided do not cover a representative sample of all possible substrates, or even of all possible saccharides. For example, it is not disclosed whether the claimed reaction can fluorinate the 2- and 3- positions of pyranose sugars such as glucose, a reactivity which would be uncertain in view of the teaching of Dmowski et al. on the inability of similar fluorinating agents to fluorinate cyclohexanol.

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art such as the prediction of the reactivity of novel compounds. See MPEP 2164.

The quantity of experimentation necessary: In order to determine the reactivity or lack thereof against all possible substrates, one skilled in the art would undertake to test the claimed fluorinating agents against a representative sample of possible substrates. This sample would include a broad diversity of compounds having vastly different structures and functional groups. Testing these substrates would require the synthesis of a large number of novel, structurally distinct compounds, which is in itself an unpredictable experimental undertaking.

Furthermore, given the lack of existing knowledge in the prior art as to the full scope of the reactivity of microwave-promoted fluorinations involving the claimed substrates, one skilled in the art would not be able to predict which substrates are or are not worth investigating, but would rather have to investigate the full diversity of substrate types. Thus practicing the claimed invention requires an undue burden of unpredictable experimentation.

*Genentech*, 108 F.3d at 1366, states that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors, as discussed above, particularly the breadth of the claims and the lack of guidance, Applicants fail to provide information sufficient to practice the claimed invention for the fluorination of all possible substrates.

Claims 4, 5, 18, and 21-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of fluorination involving an active agent of formula I or II, or a complex of HF with an alkylamine, does not reasonably provide enablement for a method involving any fluorinating agent whatsoever. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a

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disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: The claimed invention is a reaction method comprising fluorinating a substrate with a fluorinating agent.

The state of the prior art: The general classes of fluorinating agents claimed in formulas I and II are known in the art as sources of nucleophilic fluorine, as are those included in the scope of claims 19-20. However, the art does not exhaustively teach the full scope of all compounds which are capable of fluorinating a substrate under microwave irradiation.

Microwave irradiation has been shown in the art to promote nucleophilic displacement by fluoride in fluorination reactions similar to the ones claimed, leading to shorter reaction times. However, the prior art does not give an reason to expect that microwaves will be compatible with all nucleophilic fluorinations or with all possible fluorination reactions. For example, sulfur hexafluoride, DAST, molecular fluorine, and xenon tetrafluoride have not been characterized under microwave irradiation as fluorination reagents.

The relative skill of those in the art: The relative skill of those in the art is high.



The predictability or unpredictability of the art: Different reactants have different substrate specificity, as well as different stereo- and regioselectivity. It cannot be assumed that all reactants which perform a particular class of chemical transformation such as fluorination will all behave similarly under various conditions such as microwave irradiation. Furthermore, it is not possible based on the current state of the art to predict in advance the full range of compounds which are capable of acting as fluorinating agents. Thus the discovery and design of new fluorinating agents is highly unpredictable.

The Breadth of the claims: The scope of claims 4 and 5 includes all compounds capable of transferring a fluorine atom to any other compound under any reaction conditions. The scope of claims 18 and 21-23 includes all such compounds which can be made by reacting hydrofluoric acid with a base.

The amount of direction or guidance presented: The instant specification concerns compounds of the formulas I and II as disclosed in the instant claims. It does not describe fluorinating agents generally, provide the full scope of all fluorinating agents, or allow one skilled in the art to determine which fluorinating agents can be enhanced by microwave irradiation.

The presence or absence of working examples: Working examples are provided for certain specific fluorinating agents, namely those of formula I and II, as well as certain HF-amine complexes. These are not representative of all possible fluorinating agents.

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art such as the discovery of novel compounds and reactions. See MPEP 2164.

The quantity of experimentation necessary: In order to determine the reactivity or lack thereof of all possible fluorinating agents, one skilled in the art would undertake to test a representative sample of all possible fluorinating agents against a representative sample of substrates under microwave irradiation. This sample would include a broad diversity of potential fluorinating agents having vastly different structures and functional groups. Testing these substrates would require the synthesis of a large number of novel, structurally distinct compounds, which is in itself an unpredictable experimental undertaking.

Furthermore, given the lack of existing knowledge in the prior art as to the full scope of the reactivity of microwave-promoted fluorinations involving various fluorinating agents, one skilled in the art would not be able to predict which substrates are or are not worth investigating, but would rather have to investigate the full diversity of possible fluorinating agents. Thus practicing the claimed invention requires an undue burden of unpredictable experimentation.

*Genentech*, 108 F.3d at 1366, states that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors, as discussed above, particularly the scope of the claims and the lack of guidance, Applicants fail to provide information sufficient to practice the claimed invention for all possible fluorinating agents.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 4, 5, 18, and 21-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Chirakal et al. (Reference included with PTO-892) Chirakal et al. discloses a method of fluorinating a carbohydrate comprising heating  $^{18}\text{F}^-$  with  $\text{K}_2\text{CO}_3$  or  $\text{KHCO}_3$  and a 2,2,2 cryptand ligand in the presence of the carbohydrate substrate mannose triflate under microwave irradiation. (p. 150, left column, second paragraph) The microwave irradiation was carried out using a domestic microwave oven. (p. 149, left column, first paragraph) Because domestic microwave ovens use a frequency of about 2.5 GHz, this irradiation falls within the limits of instant claim 5. Furthermore, fluoride combined with  $\text{KHCO}_3$  is reasonably considered to be a complex of HF with a base according to instant claim 18, and the 2,2,2-crypt ligand is reasonably considered to be an agent accelerating a reaction according to instant claim 21. Thus the claimed invention is anticipated by Chirakal et al.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1 and 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dmowski et al. (Reference included with PTO-892) Dmowski et al. discloses a fluorinating agent difluorobenzyldimethylamine (DBDA). (p. 219, last paragraph) DBDA falls within the limitations of formula I in instant claim 1. DBDA is disclosed to be useful for the dehydrofluorination of primary alcohols, for example. (p. 221, first paragraph) Dmowski et al. does not disclose a method of fluorinating a saccharide using DBDA.

It would have been obvious to one of ordinary skill in the art at the time of the invention to fluorinate the primary alcohol of a saccharide using DBDA. (e.g. the 6-position of glucose) One of ordinary skill in the art would have been motivated to practice the invention in this manner because this position is a primary alcohol and DBDA is already disclosed to be useful for the dehydrofluorination of primary alcohols. One of ordinary skill in the art would reasonably have expected success because fluorinating the primary alcohol position of a saccharide is already included within the broad teaching of Dmowski et al. with respect to primary alcohols and because adapting a disclosed prior art reaction to a specific substrate having the same functionality is well within the ordinary and routine level of skill in the art.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 and 5-6 of U.S. Patent No. 7019173. (cited in PTO-892, herein referred to as '173) Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims 1-3 are an obvious specie of the claimed genus of claims 1-3 and 5-6 of '173.

Claims 1-3 and 5 of '173 are drawn to a method of fluorinating a substrate using a compound which is the same as the compound of formula I recited in instant claim 1. Claim 6 of '173 further limits the active group to a primary alcohol. Claims 1-3 and 5-6 of '173 do not explicitly claim a method of fluorinating a saccharide.

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the method of claims 1-3 and 5-6 of '173 on a saccharide as a substrate. One of ordinary skill in the art would have been motivated to practice the invention in this manner because a saccharide is a primary alcohol as recited by claim 6 of '173. One of ordinary skill in the art would have reasonably expected success because adapting a reaction to a specific embodiment of a general teaching is well within the ordinary and routine level of skill in the art.

Claims 4-11 and 24 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 and 5 of copending Application No. 10/591698. (Cited in PTO-892, herein referred to as '698) Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are anticipated by claims 1-3 and 5 of '598.

Claims 1 and 2 of '698 is drawn to a method of fluorination comprising reacting a compound of general formula (I), which is the same between the instant application and '698, with a substrate. The substrate is a hydroxyl compound, and in one embodiment where  $n=0$ , is a diol. Claims 3 and 5 of '698 are drawn to methods in which the reaction is accelerated by microwave irradiation, as is the case in the claimed invention. Thus claims 1-3 and 5 of '698 anticipate the claimed invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

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### Conclusion

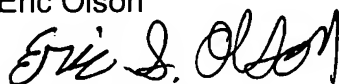
No claims are allowed in this application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

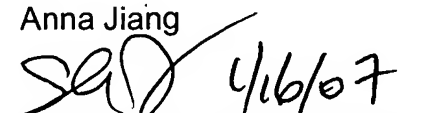
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Eric Olson



Patent Examiner  
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